

## *REMARKS*

### *The Pending Claims*

Claims 1-26 are currently pending and directed to a liquid composition for maintaining a non-enveloped viral vector (claims 1-14), a method of preserving a non-enveloped viral vector in the liquid composition (claims 15-18), and a method of administering a non-enveloped viral vector particle to a host cell comprising contacting a host cell with the liquid composition (claims 19-26).

### *The Amendments to the Claims*

Claim 5 has been amended to point out more particularly and claim more distinctly the present invention. Specifically, claim 5 has been amended to correct dependency. No new matter has been added by way of this amendment.

### *The Office Action*

The Office has rejected claims 5 and 6 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Office has rejected claims 1-7, 9, 11, and 13 under 35 U.S.C. § 102(a) as allegedly anticipated by Evans et al. (WO 01/66137) and under 35 U.S.C. § 102(e) as allegedly anticipated by Evans et al. (US 2002/0041881 A1). Claims 1-14 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of Kuma et al. (EP 0872249 A1), Herrmann et al. (US 5,792,643), Evans et al. (US 2002/0041881 A1), Evans et al. (WO 01/66137), Kovesdi et al. (WO 00/34444), and/or Frei et al. (WO 99/41416). Claims 1-14 also have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-24 of US 6,514,943 (Kovesdi et al.) or claims 13-20 of US 6,225,289 943 (Kovesdi et al.) in view of the Evans references.

### *Restriction Requirement and Election*

The Office has set forth a restriction requirement. In particular, the Office Action has set forth three groups of claims: (i) claims 1-14, drawn to a composition (class 424, subclass 600), (ii) claims 15-18, drawn to a method of preserving a viral vector (class 435, subclass 400), and (iii) claims 19-26, drawn to a method for administering a viral vector (class 424, subclass 204.1), and requires election of a "single invention" for further prosecution. Applicants confirm the provisional election, with traverse, of claims 1-14, drawn to a composition. Reconsideration of the requirement for restriction is respectfully requested.

*Discussion of the Restriction Requirement*

There are two separate criteria for a proper requirement for restriction between patentably distinct inventions: (i) the inventions must be independent or distinct as claimed, *and* (ii) there must be a serious burden on the Examiner if restriction is not required. Both of these criteria must exist for a restriction requirement to be proper, and “[i]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, *even though it includes claims to distinct or independent inventions*” (M.P.E.P. § 803, emphasis added).

In the case at hand, the Office fails to meet the above-identified criteria and to present the required supporting evidence and reasoning. There is significant overlap in subject matter between the groups of claims, such that references considered during the examination of the claims of one group would be considered during the examination of the claims of another group. For example, references identified by a search of art relevant to the composition claims of Group (i) also could be relevant to the method claims of Groups (ii) and (iii). In this regard, Applicants point out that the claims of Groups (i) and (iii) are classified in the same class. This is not to say that the claims stand or fall together. Rather, the overlap in the relevance of references and the overlap in the classification of the claimed subject matter suggests that there is no need for a restriction requirement.

Thus, the Office has failed to meet the criteria for a proper requirement for restriction. Applicant respectfully submits that the requirement for restriction is improper and should be withdrawn.

*Discussion of the Rejection under Section 112, second paragraph*

The Office contends that claim 5 is indefinite because “the nonionic surfactant” lacks antecedent basis. Claim 5 has been amended to depend from claim 4. As such, the indefiniteness rejection is believed to be moot.

The Office contends that claim 6 is indefinite because it is unclear if “FFU/mL” is intended to mean “PFU/mL.” As described at page 6, paragraph [0020], of the specification, preferably, the number of particles is measured in terms of focus forming units (FFU). FFU represents the number of focuses formed by infected cells and is determined by means of an optical microscope using standard protocols. FFU/mL can be measured using any suitable technique for determining FFU/mL. As such, the indefiniteness rejection is improper and should be withdrawn.

*Discussion of the Rejection under Sections 102(a) and 102(e)*

The Office contends that claims 1-7, 9, 11, and 13 are anticipated by the Evans references. Applicants traverse these rejections for the following reasons.

The invention is directed to a composition for maintaining a non-enveloped viral vector, a method of preserving a non-enveloped viral vector in the composition, and a method of administering a non-enveloped viral vector particle to a host cell comprising contacting a host cell with the composition. The composition comprises (a) about 1-25% trehalose, (b) about 0.05-2 mM of a divalent metal salt and/or a cationic polymer, (c) a multiplicity of non-enveloped viral vector particles, and (d) a liquid carrier.

The Evans references do not disclose or suggest the specific composition described above. While the Evans references disclose the use of cryoprotectants and include trehalose among a list of cryoprotectants, a particular amount of trehalose to be used in the composition is not described. Specifically, the Evans references only disclose particular amounts of sorbitol and sucrose to be used in the composition and do not disclose a composition comprising 1-25% trehalose, as recited in the pending claims.

As such, the Evans references do not teach each and every element of the pending claims, and the anticipation rejections should be withdrawn.

*Discussion of the Section 103(a) and Obviousness-Type Double Patenting Rejections*

The Office contends that claims 1-14 are obvious in view of one or more of several references, or combinations thereof, as discussed below. Applicants traverse these rejections for the following reasons.

Kuma et al.

The Office contends that the Kuma reference discloses a composition for preserving viruses comprising 1-10% trehalose, 1-10% arginine, a cationic polymer (e.g., polyethylene glycol), a buffer, and adenovirus.

The Kuma reference does not teach or suggest a composition comprising 0.05-2 mM of a divalent metal salt, cationic polymer, or combination thereof, as recited in the pending claims. While the Kuma reference discloses the addition of a cationic polymer to the composition, there is no teaching or suggestion within the Kuma reference of the particular amount of a cationic polymer required by the pending claims.

Therefore, the Kuma reference does not disclose nor suggest all the elements of the pending claims and cannot itself properly form the basis of a *prima facie* obviousness rejection.

Herrmann et al.

The Herrmann reference does not teach or suggest a composition comprising 0.5-2 mM of a divalent metal salt, cationic polymer, or combination thereof, as recited in the pending claims. While the Herrmann reference discloses the addition of a “neutral salt” which includes sodium chloride, potassium chloride, or magnesium chloride (see col. 7, lines 4-6, of the Herrmann reference), there is no teaching or suggestion within the Herrmann reference of the particular amount of a divalent salt required by the pending claims.

Therefore, the Herrmann reference does not disclose nor suggest all the elements of the pending claims and cannot itself properly form the basis of a *prima facie* obviousness rejection.

Evans et al.

As described above, the Evans references do not teach or suggest the particular amount of trehalose to use in a liquid composition for preserving viruses, as recited in the pending claims. In instances where a specific amount of another cryopreservant is described, e.g., sorbitol and sucrose, the amounts differ based on the salt concentration of the composition (see, e.g., page 4, paragraph [0056], of US 2002/0041884 A1). Therefore, it would not have been obvious for one of ordinary skill in the art to select the particular amount of trehalose recited in the pending claims based on the disclosure of the Evans references.

Additionally, the Office contends that it would have been obvious for one of ordinary skill in the art to arrive at the composition of the present invention by combining the disclosures of the Evans references with the disclosures of US 6,514,943 (Kovesdi et al., “the Kovesdi ‘943 patent”) or US 6,225,289 (Kovesdi et al., “the Kovesdi ‘289 patent”). Moreover, the Office contends that claims 1-14 of the subject application are unpatentable – in terms of obviousness-type double patenting – over claims 12-24 of the Kovesdi ‘943 patent or claims 13-20 of the Kovesdi ‘289 patent in view of the Evans references.

The Kovesdi ‘943 and ‘289 patents do not describe the inclusion of 0.05-2 mM of a divalent metal salt, a cationic polymer, or a combination thereof, in a composition comprising trehalose, as required by the pending claims. The Kovesdi ‘943 patent discloses a composition comprising 3% sucrose in combination with 10 mM MgCl<sub>2</sub> (see, e.g., Example 5 of the Kovesdi ‘943 patent), but the amount of MgCl<sub>2</sub> is outside of the range recited in the pending claims and the composition does not comprise trehalose as required by the pending claims.

As described above, the Evans references do not describe specific amounts of trehalose to be included in the composition, but rather only disclose specific composition ranges of sorbitol and sucrose. The Kovesdi '943 and '289 patents also disclose sucrose in compositions (e.g., with  $\text{MgCl}_2$  in Example 5 of the Kovesdi '943 patent). Therefore, the combination of the disclosures of the Kovesdi '943 and/or '289 patents (or the specified claims of the Kovesdi '943 and/or '289 patents) with the disclosures of the Evans references would result in the preparation by one of ordinary skill in the art of a composition comprising the particular amounts of sucrose and  $\text{MgCl}_2$  recited in those references, rather than the composition of the pending claims.

As such, the subject matter of the pending claims cannot be considered to be unpatentable over the Evans references alone or in combination with the Kovesdi '943 and/or '289 patents.

Kovesdi et al.

The Office contends that WO 00/34444 (Kovesdi et al., "the Kovesdi '444 PCT") discloses the use of divalent metal salts in the composition (see Office Action, page 12). Specifically, the Office contends that the Kovesdi '444 PCT discloses  $\text{NaCl}$  as a divalent metal salt (see Office Action, page 12). Presumably, the Office meant to refer to the 10 mM  $\text{MgCl}_2$  disclosed in the composition comprising 3% sucrose of Example 5, since  $\text{NaCl}$  is a monovalent salt. However, the composition containing the  $\text{MgCl}_2$  disclosed in the Kovesdi '444 PCT does not include trehalose as recited in the pending claims.

Moreover, the combination of the disclosure of the Kovesdi '444 PCT with the disclosures of the Evans references does not necessarily yield the present invention as defined by the pending claims. The Evans references disclose that sucrose is a preferred cryopreservant, and particular amounts of sucrose with  $\text{MgCl}_2$  in the composition are specified by the Evans reference, as well as the Kovesdi '444 PCT (see, e.g., Example 5). As discussed above, while trehalose is mentioned as a potential cryopreservant for inclusion in the compositions of the Evans references, no amount of trehalose is specified in the compositions of the Evans references. Indeed, the Evans references only describe specific composition ranges for sorbitol and sucrose, which vary based on the salt concentration of the composition. Thus, the combination of the disclosures of the Kovesdi '444 PCT and the Evans references would result in the preparation by one of ordinary skill in the art of a composition comprising sucrose and  $\text{MgCl}_2$  in the amounts recited in these references, rather than the composition recited in the pending claims.

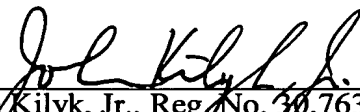
Additionally, one of ordinary skill in the art would not have necessarily arrived at the present invention as recited in the pending claims by combining the disclosure of the Kovesdi '444 PCT with that of the Frei reference. As described above, the Kovesdi '444 PCT does not describe the use of a divalent metal salt, a cationic polymer, or a combination thereof in a composition comprising trehalose; rather the Kovesdi '444 PCT discloses the use of  $MgCl_2$  in combination with sucrose. The Frei reference does not disclose the use of trehalose in the composition for preserving viruses, but rather lists sucrose as a preferred polyhydroxy hydrocarbon. Additionally, all of the compositions described in the Examples of the Frei reference include sucrose (see, e.g., pages 9-10). While the Frei reference describes the use of divalent metal salts in the composition, there is no disclosure in the Frei reference of a composition comprising a divalent metal salt and trehalose. Therefore, if one of ordinary skill in the art had prepared a composition based on the combination of the disclosures of the Frei reference and the Kovesdi '444 PCT, the resulting composition would have been a composition comprising sucrose and a divalent metal salt, not the composition defined by the pending claims.

For the foregoing reasons, the subject matter defined by claims 1-14 cannot be considered unpatentable in view of the above-cited references, or combinations thereof, and the obviousness rejections should be withdrawn.

### *Conclusion*

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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